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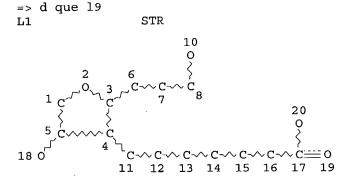
STRUCTURE FILE UPDATES: 29 JUN 2004 HIGHEST RN 701199-61-3 DICTIONARY FILE UPDATES: 29 JUN 2004 HIGHEST RN 701199-61-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html



NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

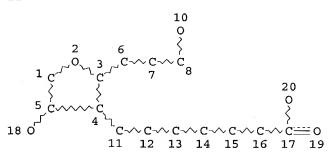
GRAPH ATTRIBUTES:
RSPEC 3
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L2 86 SEA FILE=REGISTRY SSS FUL L1
L6 138293 SEA FILE=REGISTRY ABB=ON PLU=ON C5-C6/ES
L7 2566128 SEA FILE=REGISTRY ABB=ON PLU=ON (OC4-C6 OR SC4-C6 OR NC4-C6 OR C6-C6 OR OC5-C6 OR SC5-C6 OR NC5-C6)/ES
L8 2696270 SEA FILE=REGISTRY ABB=ON PLU=ON L7 OR L6
L9 0 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND L8

=> d que 110

L1



STR

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 3

NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L2 86 SEA FILE=REGISTRY SSS FUL L1

L10 29 SEA FILE=REGISTRY ABB=ON PLU=ON 46.150.18/RID AND L2

=> b hcaplus

FILE 'HCAPLUS' ENTERED AT 16:12:49 ON 30 JUN 2004
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FILE COVERS 1907 - 30 Jun 2004 VOL 141 ISS 1 FILE LAST UPDATED: 29 Jun 2004 (20040629/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que 111 nos

L1 STR

L2 86 SEA FILE=REGISTRY SSS FUL L1

L10 29 SEA FILE=REGISTRY ABB=ON PLU=ON 46.150.18/RID AND L2

L11 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L10

=> d all fhitstr l11 1-15

```
L11
    ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
     2003:97284 HCAPLUS
DN
     138:142172
ED
     Entered STN: 07 Feb 2003
     Prostaglandin analogues for promotion of hair growth
TI
IN
     Cagle, Gerald D.; Bergamini, Michael V. W.
PA
     Alcon, Inc., Switz.
SO
     PCT Int. Appl., 34 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K007-00
CC
     62-3 (Essential Oils and Cosmetics)
FAN.CNT 1
     PATENT NO.
                     KIND DATE
                                           APPLICATION NO. DATE
                            -----
                                           -----
PI
     WO 2003009820
                       A2
                            20030206
                                           WO 2002-US23584 20020725
     WO 2003009820
                       Α3
                            20030424
     WO 2003009820
                            20031113
                      B1
         W: AU, BR, CA, CN, GB, JP, MX, US
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, SK, TR
     EP 1408913
                            20040421
                      A2
                                           EP 2002-768349
                                                            20020725
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI, CY, TR, BG, CZ, EE, SK
     US 2003199590
                            20031023
                                           US 2002-275543
                      A1
                                                            20021106
PRAI US 2001-307835P
                       P
                            20010725
                     P
     US 2002-373300P
                            20020417
     WO 2002-US23584
                       W
                            20020725
os
     MARPAT 138:142172
AB
     Methods and compns. for the promotion of hair growth in mammals,
     comprising PGF2\alpha analogs are disclosed. A hair growth stimulant
     composition contained travoprost 0.004, dextran-70 0.1, hydroxypropyl Me
     cellulose 0.3, NaCl 0.77, KCl 0.12, Na2EDTA 0.05, benzalkonium chlorides
     0.01, HCl and/or NaOH q.s. to pH 7.2-7.5, and purified water balance to
     100 %.
    hair growth stimulant prostaglandin FP agonist; travoprost hair growth
ST
     stimulant
ΙT
    Hair preparations
        (growth stimulants; prostaglandin analogs for promotion of hair growth)
IT
     Prostanoid receptors
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (type FP; prostaglandin analogs for promotion of hair growth)
     551-11-1D, PGF2α, analogs 130209-82-4, Latanoprost
IT
                             470455-84-6 494760-29-1
    Travoprost 192992-26-0
     494760-30-4 494760-31-5
                              494760-32-6 494760-33-7
    RL: COS (Cosmetic use); PAC (Pharmacological activity); BIOL (Biological
     study); USES (Uses)
        (prostaglandin analogs for promotion of hair growth)
IT
    192992-26-0
    RL: COS (Cosmetic use); PAC (Pharmacological activity); BIOL (Biological
    study); USES (Uses)
        (prostaglandin analogs for promotion of hair growth)
RN
    192992-26-0 HCAPLUS
    L-altro-Oct-3-enitol, 5,8-anhydro-1-0-(3-chlorophenyl)-3,4,6-trideoxy-6-
     [(2Z)-7-(1-methylethoxy)-7-oxo-2-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry. Double bond geometry as shown.

L11 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:84603 HCAPLUS

DN 136:129085

ED Entered STN: 31 Jan 2002

TI Use of nonsteroidal anti-inflammatory agents in combination with compounds that have FP prostaglandin agonist activity to treat glaucoma and ocular hypertension

IN Hellberg, Mark R.; Nixon, Jon C.

PA Alcon Manufacturing, Ltd., USA

SO U.S., 10 pp., Cont.-in-part of U.S. 6,066,671. CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-215

NCL 514530000

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 3

FAN.CNT 3						
PATENT NO.		KIND	DATE	APPLICATION NO.	DATE	
	ΡI	US 6342524	B1	20020129	US 2000-575833	20000522
		US 6066671	Α	20000523	US 1997-994903	19971219
		PT 1039895	${f T}$	20021031	PT 1998-960732	19981204
		ES 2178291	Т3	20021216	ES 1998-960732	19981204
		US 2002103255	A1	20020801	US 2002-59692	20020128
		US 6646001	B2	20031111		
	PRAI	US 1997-994903	A2	19971219		
		US 2000-575833	A2	20000522		

OS MARPAT 136:129085

AB Methods and compns. are provided for the treatment of glaucoma and ocular hypertension, comprising the administration of a prostaglandin analog (e.g. travoprost) and a prostaglandin synthesis inhibitor (e.g. nepafenac).

ST prostaglandin analog combination glaucoma ocular hypertension; prostaglandin synthesis inhibitor combination glaucoma; travoprost nepafenac glaucoma pharmaceutical

IT Prostaglandins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (F, agonists; nonsteroidal anti-inflammatory agents in combination with compds. having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)

IT Prostaglandins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(analogs; nonsteroidal anti-inflammatory agents in combination with compds. having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)

- IT Antiglaucoma agents
 - (nonsteroidal anti-inflammatory agents in combination with compds. having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)
- IT Anti-inflammatory agents
 - (nonsteroidal; nonsteroidal anti-inflammatory agents in combination with compds. having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)
- IT Drug delivery systems
 - (ophthalmic; nonsteroidal anti-inflammatory agents in combination with compds. having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)
- TT 78281-72-8, Nepafenac 78281-73-9 78281-77-3 120373-36-6, Unoprostone 130209-82-4, Latanoprost 157283-68-6, Travoprost 192992-28-2 392230-89-6 392230-90-9
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 - (Biological study); USES (Uses)
 - (nonsteroidal anti-inflammatory agents in combination with compds. having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)
- RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD RE
- (1) Adam; Human Molecular Genetics 1997, V6(12), P2091 HCAPLUS
- (2) Akarsu; Human Molecular Genetics 1996, V5(8), P1199 HCAPLUS
- (3) Alm; Current Opinion in Ophthalmology 1993, V4(11), P44
- (4) Andersen; Arch Ophthalmol 1997, V115, P384 MEDLINE
- (5) Anon; GB 2059963 A 1981 HCAPLUS
- (6) Anon; EP 0221753 A2 1987 HCAPLUS
- (7) Anon; WO 9208465 1992 HCAPLUS
- (8) Anon; WO 9517178 1995 HCAPLUS
- (9) Anon; WO 9614411 1996 HCAPLUS
- (10) Anon; WO 9640102 1996 HCAPLUS
- (11) Anon; WO 9640103 1996 HCAPLUS
- (12) Anon; WO 0025771 2000 HCAPLUS
- (13) Bishop; US 5510383 A 1996 HCAPLUS
- (14) Clark; Emerging Drugs 1999, V4, P333 HCAPLUS
- (15) Clark; Invest Ophthalmol Vis Sci 1994, V35, P281 MEDLINE
- (16) Desantis; US 5565492 A 1996 HCAPLUS
- (17) Desantis; US 5627209 A 1997 HCAPLUS
- (18) Giuffre; Graefe's Archive Ophthalmology 1985, V222, P139 MEDLINE
- (19) Graff; Hum Genet 1995, V96, P285 MEDLINE
- (20) Hellberg; US 5607966 A 1997 HCAPLUS
- (21) Hellberg; US 5698733 A 1997 HCAPLUS
- (22) Hellberg; US 5750564 A 1998 HCAPLUS
- (23) Hellberg; US 5925673 A 1999 HCAPLUS
- (24) Kerstetter; American Journal of Ophthalmology 1988, V105, P30 HCAPLUS
- (25) Klimko; US 5665773 A 1997 HCAPLUS
- (26) Klimko; US 5807892 A 1998 HCAPLUS
- (27) Kubota; Genomics 1997, V41, P360 HCAPLUS
- (28) Meyer; Hum Genet 1996, V98, P567 HCAPLUS
- (29) Miyake; Arch Ophthl 1999, V117(1), P34 HCAPLUS
- (30) Morissette; Am J Hum Genet 1995, V56, P1431 HCAPLUS
- (31) Nakajima; Graefe's Archive Ophthalmology 1991, V229, P411 MEDLINE
- (32) Nguyen; US 5606043 A 1997 HCAPLUS
- (33) Ortego; FEBS Letters 1997, V413, P349 HCAPLUS
- (34) Polansky; US 5474985 A 1995 HCAPLUS
- (35) Polansky; US 5599535 A 1997 HCAPLUS
- (36) Polansky; Glaucoma Update IV 1991
- (37) Polansky; Ophthalmologica 1997, V211, P126 HCAPLUS
- (38) Richards; Am J Hum Genet 1994, V54, P62 HCAPLUS

- (39) Rozsival; Current Eye Research 1981, V1, P391 MEDLINE
- (40) Sallee; US 5721273 A 1998 HCAPLUS
- (41) Sallman; US 6107343 A 2000 HCAPLUS
- (42) Sarfarazi; Genomics 1995, V30, P171 HCAPLUS
- (43) Schwartz; Arch Ophthalmol 1987, V105, P1060 MEDLINE
- (44) Selliah; US 5814660 A 1998 HCAPLUS
- (45) Selliah; US 5866602 A 1999 HCAPLUS
- (46) Selliah; US 5994397 A 1999 HCAPLUS
- (47) Selliah; US 6025392 A 2000 HCAPLUS
- (48) Sheffield; Nature Genetics 1993, V4, P47 HCAPLUS (49) Sommer, A; Arch Ophthalmol 1991, V109, P1090 MEDLINE
- (50) Stjernschantz; US 5422368 A 1995 HCAPLUS
- (51) Stoilova; Genomics 1996, V36, P142 HCAPLUS
- (52) Stone; Science 1997, V275, P668 HCAPLUS
- (53) Sunden; Genome Research 1996, V6, P862 HCAPLUS
- (54) Ueno; US 5151444 A 1992 HCAPLUS
- (55) Wiggs; Genomics 1994, V21, P299 HCAPLUS
- (56) Wilson; Cur Eye Res 1993, V12, P783 MEDLINE
- (57) Wirtz; Am J Hum Genet 1997, V60, P296 HCAPLUS
- (58) Woodward; US 5093329 A 1992 HCAPLUS
- (59) Yanni; US 5475034 A 1995 HCAPLUS
- (60) Yanni; US 6066671 A 2000 HCAPLUS
- (61) Zinke; US 6169111 B1 2001 HCAPLUS
- (62) Zinke; US 6172109 B1 2001 HCAPLUS
- 192992-28-2
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 - (Biological study); USES (Uses)
 - (nonsteroidal anti-inflammatory agents in combination with compds.
 - having FP prostaglandin agonist activity to treat glaucoma and ocular hypertension)
- 192992-28-2 HCAPLUS RN
- CN L-altro-Oct-3-enitol, 5,8-anhydro-1-0-(3-chlorophenyl)-3,4,6-trideoxy-6-[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

- ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
- AN 2002:11126 HCAPLUS
- DN 136:85723
- ED Entered STN: 04 Jan 2002
- Process and preparation of novel intermediates for an 11-oxa prostaglandin ΤI
- Delgado, Pete; Conrow, Raymond E.; Dean, William D.; Gaines, Michael S. IN
- PA
- SO U.S. Pat. Appl. Publ., 12 pp. CODEN: USXXCO
- DT Patent

LA English

IC ICM C07D409-02

ICS C07D333-72; C07D037-32

NCL 546152000

CC 26-3 (Biomolecules and Their Synthetic Analogs)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO	. DATE
PI	US 2002002284	A1	20020103	US 2001-860772	20010518
	US 6441196√	B2	20020827		
	US 200301388/4	A1	20030116	US 2002-227912	20020826
	US 6620947 √	B2	20030916		
W	US 2004063968	A1	20040401	US 2003-663855	20030916
RRAI	US 2000-205692P	P	20000519		
lg,	US 2001-860772	A1	20010518		
Ser Land	US 2002-227912	Al	20020826		
os	CASREACT 136:857	23; MA			
, at					

$$Y^1 = W$$
 or $Y^1 = W$

Improved processes and intermediates for preparation of 11-oxa prostaglandin analogs I (R = H, pharmaceutically acceptable cationic salt moiety, or CO2R forms a pharmaceutically acceptable ester moiety; R9O and R15O = same or different and constitute a free or functionally modified hydroxy group; --- = single or trans double bond; X = (CH2)p or (CH2)pO where p = 1-6; Y = (substituted)phenyl ring; or X-Y = (CH2)mY1 where m = 0-6 and W = CH2, O, S(O)x, NR1O, CH2CH2, CH=CH, CH2O, CH2S(O)x, CH=N, CH2NR1O where x = 0-2 and R1O = H, alkyl, acyl; Z = H, alkyl, alkoxy, acyl(oxy), halo, amino, OH) were accomplished. Thus II was prepared in 90% yield from D-sorbitol via III in a multistep process.

Ι

ST oxaprostaglandin analog prepn; prostaglandin oxa analog prepn; heptenoate tetrahydrofuranylhydroxy analog prepn; furan hydroxytetrahydro heptenoic

```
acid deriv prepn
IT
     Prostaglandins
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (analogs, 11-oxa; preparation of 11-oxa prostaglandin analogs)
     192992-28-2P 385842-08-0P 385842-09-1P
IT
    RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (preparation of 11-oxa prostaglandin analogs)
     50-70-4, D-Sorbitol, reactions 67-63-0, 2-Propanol, reactions
IT
                                                                       77-76-9,
                          108-43-0, 3-Chlorophenol 534-07-6,
     2,2-Dimethoxypropane
     1,3-Dichloroacetone
                          1099-45-2 2623-87-2, 4-Bromobutyric acid
     40665-94-9, Dimethyl 3-(3-chlorophenoxy)-2-oxopropyl phosphonate
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of 11-oxa prostaglandin analogs)
                 13605-66-8P
                                27299-12-3P 70923-64-7P, Isopropyl
TT
     13605-65-7P
                      73718-87-3P
                                     101069-27-6P
     4-bromobutyrate
                                                    101069-28-7P
                                                                 101125-99-9P
     159898-26-7P
                                   374680-98-5P 374680-99-6P
                   256662-69-8P
     385841-95-2P
                   385841-96-3P
                                   385841-97-4P
                                                  385841-98-5P
                                                                 385841-99-6P
                                                  385842-03-5P
     385842-00-2P
                   385842-01-3P
                                   385842-02-4P
                                                                 385842-04-6P
                   385842-06-8P 385842-07-9P
     385842-05-7P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of 11-oxa prostaglandin analogs)
IT
     192992-28-2P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (preparation of 11-oxa prostaglandin analogs)
RN
    192992-28-2 HCAPLUS
    L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-
CN
     [(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

L11

```
2001:851169 HCAPLUS
ΑN
DN
     135:371564
     Entered STN: 23 Nov 2001
ED
     Process for preparing 11-oxaprostaglandins and intermediates
TT
     Fox, Martin Edward; Jackson, Mark
IN
PA
     Chirotech Technology Limited, UK
     PCT Int. Appl., 26 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
IC
     ICM C07F007-18
```

ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

CC 26-3 (Biomolecules and Their Synthetic Analogs)

FAN.CNT 1 APPLICATION NO. DATE KIND DATE PATENT NO. -----_____ WO 2001-GB2184 20010516 WO 2001087897 20011122 A1 PΙ W: CA, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR 20030212 EP 2001-936608 20010516 EP 1282627 A1

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR

US 2003166948 A1 20030904 US

US 2003-276846 20030505

PRAI GB 2000-12249 A 20000519 WO 2001-GB2184 W 20010516

OS CASREACT 135:371564; MARPAT 135:371564

GΙ

The present invention discloses a process for the preparation of 11-oxaprostaglandin derivs. [I; R1 = vinyl, trialkylsilylethynyl, formyl protected as an acetal, protected hydroxymethyl group; R2 = alkyl, aryloxy, alkoxy; R3-R6 = alkyl, aryl; dashed bond = single or double bond] and intermediates thereof. Thus, oxaprostaglandin derivative II was prepared via multistep synthetic sequence starting from Me (R)-(4-tert-butyldimethylsilyloxy)-3-hydroxybutanoate, trimethylsilylpropargyl bromide, allyl bromide and (E)-1-iodo-4-(3-chlorophenoxy)-3-tert-butyldimethylsilyloxy-1-butene.

ST prostaglandin oxa intermediate prepn

IT Asymmetric synthesis and induction

(of 11-oxaprostaglandins and intermediates)

IT Prostaglandins

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of 11-oxaprostaglandins and intermediates)

IT Coupling reaction

(stereoselective; in preparation of 11-oxaprostaglandins and intermediates)

IT 15489-27-7

RL: CAT (Catalyst use); USES (Uses)

(preparation of 11-oxaprostaglandins and intermediates) 374680-86-1P 374680-87-2P 374680-88-3P 256662-69-8P 374680-85-0P IT 374680-91-8P 374680-92-9P 374680-93-0P 374680-90-7P 374680-89-4P 374680-98-5P 374680-96-3P 374680-97-4P 374680-95-2P 374680-94-1P 374680-99-6P RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of 11-oxaprostaglandins and intermediates) 374681-02-4P IT 192992-28-2P RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of 11-oxaprostaglandins and intermediates) 75-77-4, Trimethylsilyl chloride, reactions 106-95-6, Allyl bromide, TT 603-35-0, Triphenylphosphine, reactions 18162-48-6 38002-45-8, Trimethylsilylpropargyl bromide 40949-94-8, Potassiumbis (trimethylsilyl) amide 70923-64-7, Isopropyl 4-bromobutyrate 374681-00-2 374681-01-3 374681-03-5 133095-91-7 RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of 11-oxaprostaglandins and intermediates) IT 374681-04-6P RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of 11-oxaprostaglandins and intermediates) THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT RE (1) Alcon Lab Inc; WO 9723223 A 1997 HCAPLUS (2) Alcon Lab Inc; WO 9821182 A 1998 HCAPLUS 374680-99-6P TT RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of 11-oxaprostaglandins and intermediates) RN374680-99-6 HCAPLUS L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-2,7-CN bis-O-[(1,1-dimethylethyl)dimethylsilyl]-6-[(3Z)-7-(1-methylethoxy)-7-oxo-

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

L11 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:114400 HCAPLUS

DN 132:151597

ED Entered STN: 17 Feb 2000

TI Preparation and formulation of tetrahydrofuran prostaglandin analogs for use as ocular hypotensives

```
IN Selliah, Robert D.; Hellberg, Mark R.; Klimko, Peter G.; Sallee, Verney
L.; Zinke, Paul W.
```

PA Alcon Laboratories, Inc., USA

SO U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 809,920. CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-34 ICS C07D307-20

NCL 514473000

CC 26-3 (Biomolecules and Their Synthetic Analogs) Section cross-reference(s): 1, 2, 63

FAN.CNT 2

	PATENT NO.	KIND DA	ATE	APPLICATION NO.	DATE
ΡI	US 6025392	A 20	0000215	US 1998-109852	19980702
	WO 9723223	A1 19	9970703	WO 1996-US17900	19961112
	W: AU, CA,	CN, JP, M	MX, US		
	RW: AT, BE,	CH, DE, I	DK, ES, FI,	FR, GB, GR, IE, IT,	, LU, MC, NL, PT, SE
	US 5994397	A 19	9991130	US 1997-809920	19970404
PRAI	US 1995-9866P	P 19	9951222		
	WO 1996-US17900	W 19	9961112		
	US 1997-809920	A2 19	9970404		
os	MARPAT 132:15159	97			
GI				•	

- AB THF analogs of F-series prostaglandins, such as I [R = carboxyalkyl, amidoalkyl, hydroxyalkyl, etc.; R2, R3 = H, F, OH, etc.; R4 = phenoxyalkyl, phenylalkyl, etc.; R25 = H, acyl, alkyl; Y = cis-CH2CH:CH, cis-CH:CHCH2, (CH2)3; Z = C.tplbond.C, trans-CH:CH, (CH2)2], were prepared for use in treating glaucoma and ocular hypertension. Thus, THF prostanoids II (R = (CH2)nCO2CHMe2, n 2, 3) were both prepared in a multistep synthetic sequence starting from 1,2-O-isopropylidene- α -D-xylofuranose. A formulation for eye drops containing II (R = (CH2)2CO2CHMe2) was presented.
- ST THF prostaglandin analog prepn antiglaucoma agent; ocular hypotensive THF prostaglandin analog prepn

IT Antiglaucoma agents

(preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives)

IT Prostaglandins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prostanoids; preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives)

IT 257945-30-5P 257945-31-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives) 867-13-0, Triethyl phosphonoacetate 4009-98-7, IT (Methoxymethyl) triphenylphosphonium chloride 17814-85-6 17857-14-6 40665-94-9 20031-21-4 RL: RCT (Reactant); RACT (Reactant or reagent) (preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives) 6022-96-4P 6698-46-0P 58399-68-1P 80923-96-2P 192991-91-6P IT 192991-93-8P 192991-94-9P 192991-95-0P 192991-98-3P 192991-92-7P 192992-00-0P 192992-02-2P **192992-03-3P** 193075-40-0P 242812-27-7P 208180-29-4P 208180-30-7P 208180-62-5P 242812-26-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and formulation of THF prostaglandin analogs for use as ocular hypotensives) THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 25 RE (1) Alm; Current Opinion in Ophthalmology 1993, V4(II), P44 (2) Anon; GB 1458164 1976 HCAPLUS (3) Anon; DE 2460977 1976 HCAPLUS (4) Anon; DE 2601333 1976 HCAPLUS (5) Anon; DE 2618861 1976 HCAPLUS (6) Anon; DE 2739277 1978 HCAPLUS (7) Anon; GB 1539364 1979 HCAPLUS (8) Anon; EP 0667160 A2 1995 HCAPLUS (9) Anon: EP 0686628 A2 1995 HCAPLUS (10) Anon; WO 9526729 1995 HCAPLUS (11) Arndt; Afr J Chem 1981, V34(4), P121 HCAPLUS (12) Chan; US 5574066 1996 HCAPLUS (13) Giuffre; Graefe's Arch Clin Exp Ophthalmol 1985, V222, P139 MEDLINE (14) Hanessian; Carbohydrate Research 1985, V141, P221 HCAPLUS (15) Kerstetter; American Journal of Ophthalmology 1988, V105, P30 HCAPLUS (16) Lourens; US 4133817 1979 HCAPLUS (17) Lourens; Tetrahedron Letters 1975, V43, P3719 (18) Nakajima; Graefe's Arch Clin Exp Ophthalmol 1991, V229, P411 MEDLINE (19) Thiem; Liebigs Ann Chem 1985, V2151, P2164 (20) Thierauch; Journal of Hypertension 1994, V12, P1 HCAPLUS (21) Verdoorn; S Afr Tydskr Chem 1987, V40(2), P134 HCAPLUS (22) Vlattas; US 3883659 1975 HCAPLUS (23) Vlattas; US 4088779 1978 HCAPLUS (24) Vlattas; Tetrahedron Letters 1974, 51/52, P4451 HCAPLUS (25) Vlattas; Tetrahedron Letters 1974, 51/52, P4455 HCAPLUS 257945-30-5P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation and formulation of THF prostaglandin analogs for use as ocular

RN 257945-30-5 HCAPLUS

hypotensives)

CN L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-7-O-methyl-6-[(2Z)-7-(1-methylethoxy)-7-oxo-2-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

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ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
L11
     2000:84616 HCAPLUS
AN
DN
     132:141953
    Entered STN: 04 Feb 2000
ED
    Ophthalmic compositions containing prostaglandins and carbonic anhydrase
ΤI
     inhibitors for treatment of ocular hypertension
IN
     Ponticello, Gerald S.; Sugrue, Michael F.
    Merck & Co., Inc., USA
PA
     PCT Int. Appl., 29 pp.
SO
     CODEN: PIXXD2
     Patent
DT
     English
LA
IC
     ICM A61K031-215
     63-6 (Pharmaceuticals)
FAN.CNT 1
                                           APPLICATION NO.
                                                            DATE
     PATENT NO.
                    KIND
                            DATE
                      _ _ _ _
                            _____
                            20000203
                                           WO 1999-US16374 19990720
ΡI
     WO 2000004899
                       A1
         W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD,
             GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV,
             MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR,
             TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                           CA 1999-2337349
                                                            19990720
                       AA
                            20000203
     CA 2337349
                                           AU 1999-51144
                                                             19990720
     AU 9951144
                       Α1
                            20000214
                       A1
                            20010523
                                           EP 1999-935726
                                                            19990720
     EP 1100491
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
                            20020716
                                           JP 2000-560892
                                                             19990720
                       T2
     JP 2002521333
PRAI US 1998-119951
                            19980721
                       Α
                            19990720
     WO 1999-US16374
                       W
     Combinations of a prostaglandin, or its derivative, hypotensive lipids derived
AB
     from a prostaglandin or prostaglandin derivative or an ophthalmol. acceptable
     salt and a topical carbonic anhydrase inhibitors or their salts are
     particularly useful in the treatment of ocular hypertension and glaucoma.
     The combinations are characterized by an improved effect and reduced
     side-effects. Thus, a solution contained (S,S)-(-)-5,6-dihydro-4-ethylamino-
     6-methyl-4H-thieno-[2,3b]thiopyran-2-sulfonamide-7,7-dioxide
     monohydrochloride (carbonic anhydrase inhibitor) 22.26,
     (+)-isopropylfluprostenol (prostaglandin derivative) 10.0, sodium citrate-2H20
     2.940, benzalkonium chloride 0.075, hydroxyethyl cellulose 5.00, sodium
     hydroxide qs to ph 6.0, mannitol 16.00, and water for injection qs to 1000
     ophthalmic prostaglandin carbonic anhydrase inhibitor; ocular hypertension
ST
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prostaglandin carbonic anhydrase inhibitor

IT Antiglaucoma agents

(ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT Prostaglandins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT Drug delivery systems

(ophthalmic; ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT Lipids, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prostaglandin-derived; ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT 9001-03-0, Carbonic anhydrase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT 11138-66-2, Xanthan gum 13345-50-1, Prostaglandin A2 14152-28-4 27376-76-7 38562-01-5 53764-90-2 71010-52-1, Gellan gum 120373-24-2 120279-96-1 120373-16-2 122028-16-4 130693-82-2 138890-50-3 138890-62-7 138890-75-2 135273-39-1 138890-81-0 141115-93-7 216854-98-7 246145-93-7 256926-02-0 139066-78-7 256944-51-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

IT 256926-02-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ophthalmic compns. containing prostaglandins and carbonic anhydrase inhibitors for treatment of ocular hypertension)

RN 256926-02-0 HCAPLUS

CN L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(4-chlorophenyl)-3,4,6-trideoxy-6-[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L11 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:84614 HCAPLUS

DN 132:127751

ED Entered STN: 04 Feb 2000

TI Ophthalmic compositions containing carbonic anhydrase inhibitor, β -adrenergic antagonist, and prostaglandin for treating ocular hypertension

IN Ponticello, Gerald S.; Sugrue, Michael F.

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PA
     Merck & Co., Inc., USA
SO
      PCT Int. Appl., 34 pp.
      CODEN: PIXXD2
DT
      Patent
LA
     English
IC
     A61K031-215
      63-6 (Pharmaceuticals)
      Section cross-reference(s): 1
FAN.CNT 1
     PATENT NO.
                         KIND DATE
                                                 APPLICATION NO. DATE
     WO 2000004898
PΙ
                                20000203
                                                 WO 1999-US16143 19990716
                         A1
          W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                          AΑ
                                20000203
                                                CA 1999-2337399 19990716
     AU 9950011
                          Α1
                                20000214
                                                 AU 1999-50011
                                                                     19990716
     EP 1109546
                          A1
                                20010627
                                                 EP 1999-934101
                                                                     19990716
              AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO
      JP 2002521332
                                                 JP 2000-560891
                          T2
                                20020716
                                                                     19990716
PRAI US 1998-93594P
                          P
                                19980721
     WO 1999-US16143
                                19990716
                          W
     MARPAT 132:127751
os
     Combinations of a carbonic anhydrase inhibitor (0.5-3.0%), a
AB
     \beta-adrenergic antagonist (0.1-0.5%), and a prostaglandin or a
     prostaglandin derivative (0.03-1.0%) are particularly useful in the treatment
     of ocular hypertension (glaucoma). The combinations are characterized by
     an improved therapeutic effect and reduced side-effects. E.g., an
     ophthalmic formulation was prepared containing a carbonic anhydrase inhibitor,
     MK 507, 22.26 g, 13,14-dihydro-15-keto-20-ethyl-PGF2 iso-Pr ester 10 g,
      (S) - (-) - (tert-butylamino) - 3 - [(4-morpholino-1, 2, 5-thiadiazol-3-yl)oxy] - 2 -
     propanol maleate 6.834 g, Na citrate 2H2O 2.940 g, benzalkonium
     chloride 0.075 g, hydroxyethyl cellulose 5.00 g, NaOH as needed for pH =
     6.0, mannitol 16.00 g, and water for injection up to 1000 g. The active
     compds., phosphate buffer salts, benzalkonium chloride, and Polysorbate 80
     were added to and suspended or dissolved in water. The pH of the composition
     was adjusted to 5.5-6.0 and diluted 30 to volume  The composition was rendered
     sterile by filtration through a sterilizing filter.
     anhydrase inhibitor beta blocker prostaglandin ophthalmic glaucoma;
     antiglaucoma anhydrase inhibitor beta adrenergic antagonist prostaglandin
IT
     Antiglaucoma agents
         (ophthalmic compns. containing anhydrase inhibitor, β-blocker, and
         prostaglandin for glaucoma treatment)
IT
     Prostaglandins
     RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
     effector, except adverse); BSU (Biological study, unclassified); THU
      (Therapeutic use); BIOL (Biological study); USES (Uses)
         (ophthalmic compns. containing anhydrase inhibitor, β-blocker, and
         prostaglandin for glaucoma treatment)
     Drug delivery systems
         (ophthalmic; ophthalmic compns. containing anhydrase inhibitor,
         β-blocker, and prostaglandin for glaucoma treatment)
IT
     Drug delivery systems
         (solns., ophthalmic; ophthalmic compns. containing anhydrase inhibitor,
         β-blocker, and prostaglandin for glaucoma treatment)
```

IT Drug delivery systems

> (suspensions, ophthalmic; ophthalmic compns. containing anhydrase inhibitor, β-blocker, and prostaglandin for glaucoma treatment)

IT Adrenoceptor antagonists

 $(\beta$ -; ophthalmic compns. containing anhydrase inhibitor, β-blocker, and prostaglandin for glaucoma treatment)

9001-03-0, Carbonic anhydrase IT

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; ophthalmic compns. containing anhydrase inhibitor,

β-blocker, and prostaglandin for glaucoma treatment) IT 13345-50-1, PGA2 14152-28-4, PGA1 22664-55-7, Metipranolol 35850-13-6 33305-95-2 38562-01-5, Prostaglandin 26839-75-8, Timolol 39552-01-7, Befunolol $F2\alpha$ tromethamine salt 41639-83-2D, esters

47141-42-4, Levobunolol 118565-33-6 120279-96-1 63659-18-7, Betaxolol 120373-24-2

120373-36-6 130209-82-4 130693-82-2 134217-11-1 135273-39-1

138890-62-7 138890-84-3 139066-78-7 157283-68-6 161833-99-4 162478-72-0 164582-55-2 179937-10-1 192992-28-2

216780-87-9 216780-88-0 216780-89-1 256444-30-1

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

51781-06-7, Carteolol

53764-90-2

(ophthalmic compns. containing anhydrase inhibitor, β -blocker, and prostaglandin for glaucoma treatment)

11138-66-2, Xanthan gum 71010-52-1, Gellan gum IT

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ophthalmic compns. containing anhydrase inhibitor, β -blocker, and prostaglandin for glaucoma treatment)

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT RE

(1) Bito; US 4599353 A 1986 HCAPLUS

TT 192992-28-2

> RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ophthalmic compns. containing anhydrase inhibitor, β -blocker, and prostaglandin for glaucoma treatment)

RN192992-28-2 HCAPLUS

L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-CN [(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

L11 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

2000:10635 HCAPLUS AN

DN132:69332

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ED
     Entered STN: 06 Jan 2000
     Storage-stable prostaglandin compositions
TI
     Schneider, L. Wayne; Bawa, Rajan; Weiner, Alan L.
IN
PA
     Alcon Laboratories, Inc., USA
SO
     U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 33,748, abandoned.
     CODEN: USXXAM
DT
     Patent
     English
LA
IC
     ICM A61K031-557
NCL
     514530000
CC
     63-6 (Pharmaceuticals)
FAN.CNT 2
                                         APPLICATION NO. DATE
     PATENT NO.
                     KIND DATE
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                           _____
                      Α
PΙ
     US 6011062
                            20000104
                                          US 1999-246072
                                                           19990209
                    A
A
     US 5631287
                            19970520
                                          US 1994-362677
                                                            19941222
     US 5849792
                            19981215
                                          US 1996-738629
                      Α
                                                            19961029
                      A3
PRAI US 1994-362677
                            19941222
     US 1996-738629
                      A2
                            19961029
     US 1998-33748
                      B2
                            19980224
AΒ
     Polyethoxylated castor oils are used in prostaglandin compns. to enhance
     the chemical stability. A composition was prepared containing
(5Z) - (9R, 11R, 15R) -9-
     chloro-15-cyclohexyl-11,15-dihydroxy-3-oxa-16,17,18,19,20-pentanor-5-
     prostenoic acid iso-Pr ester and Cremophor EL.
ST
     prostaglandin compn ethoxylated castor oil
TT
     Castor oil
     RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (ethoxylated; storage-stable prostaglandin compns. containing ethoxylated
        castor oil)
     Castor oil
TТ
     RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (hydrogenated, ethoxylated; storage-stable prostaglandin compns. containing
        ethoxylated castor oil)
IT
     Polyoxyalkylenes, biological studies
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (storage-stable prostaglandin compns. containing ethoxylated castor oil)
IT
     Prostaglandins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (storage-stable prostaglandin compns. containing ethoxylated castor oil)
IT
     25322-68-3
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (storage-stable prostaglandin compns. containing ethoxylated castor oil)
     53764-90-2, PGF2\alpha isopropyl ester 130209-82-4, Latanoprost
IT
     135646-98-9, 15-Ketolatanoprost 155206-02-3 157283-66-4, Cloprostenol
     isopropyl ester
                      163075-20-5
                                    170291-05-1 170291-06-2
                                                               170291-07-3
                  170291-11-9 170291-13-1 170552-18-8
     170291-08-4
                                                            170552-20-2
     190951-81-6
                  190951-85-0
                                 190951-87-2
                                              190951-89-4
                                                            190951-91-8
     190951-93-0
                  190951-94-1
                                 190951-95-2
                                              190951-96-3
                                                            190951-97-4
     190951-98-5
                  190951-99-6 190952-00-2
                                              190952-01-3
                                                             190952-02-4
     190952-03-5 192992-26-0 246145-93-7 253436-50-9
     253436-51-0
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (storage-stable prostaglandin compns. containing ethoxylated castor oil)
RE.CNT 23
             THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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- (1) Anon; WO 8502841 1984 HCAPLUS
- (2) Anon; EP 0132027 A1 1985 HCAPLUS
- (3) Anon; EP 0330511 A2 1989 HCAPLUS
- (4) Anon; EP 0407148 A3 1991
- (5) Anon; EP 0418004 A2 1991 HCAPLUS
- (6) Anon; EP 0429248 A2 1991 HCAPLUS
- (7) Anon; EP 0435682 A2 1991 HCAPLUS
- (8) Anon; EP 0645145 A3 1995 HCAPLUS
- (9) Anon; EP 0667160 A2 1995 HCAPLUS
- (10) Anon; WO 9505163 1995 HCAPLUS
- (11) Anon; WO 9729752 1997 HCAPLUS
- (12) Anon; WO 9841208 1998 HCAPLUS
- (13) Attwood; Surfactant Systems Their Chemistry Pharmacy and Biology V11, P698
- (14) Cherng-Chyi; US 5110493 1992 HCAPLUS
- (15) DeSantis; US 5627209 1997 HCAPLUS
- (16) Foster; Arch Ophthalmol 1979, V97/9, P1703
- (17) Joose; US 4075333 1978 HCAPLUS
- (18) Nagy; US 4960799 1990 HCAPLUS
- (19) Nakajima; US 5098606 1992 HCAPLUS
- (20) Sayed; Interna'l J of Pharmaceutics 1983, V13, P302
- (21) Schneider; US 5631287 1997 HCAPLUS
- (22) Schneider; US 5849792 1998 HCAPLUS
- (23) Ushio; US 5185372 1993 HCAPLUS
- IT 192992-26-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (storage-stable prostaglandin compns. containing ethoxylated castor oil)

RN 192992-26-0 HCAPLUS

CN L-altro-Oct-3-enitol, 5,8-anhydro-1-0-(3-chlorophenyl)-3,4,6-trideoxy-6-[(2Z)-7-(1-methylethoxy)-7-oxo-2-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

- L11 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
- AN 1999:9814 HCAPLUS
- DN 130:66325
- ED Entered STN: 07 Jan 1999
- TI Keto-substituted tetrahydrofuran analogs of prostaglandins as ocular hypotensives
- IN Selliah, Robert D.
- PA Alcon Laboratories, Inc., USA
- SO PCT Int. Appl., 27 pp. CODEN: PIXXD2
- DT Patent
- LA English
- IC ICM C07C405-00 ICS A61K031-557

CC 26-3 (Biomolecules and Their Synthetic Analogs) Section cross-reference(s): 1, 63

FAN.CNT 1

	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
ΡI	WO 9857930	A1 19981223	WO 1998-US11340	19980603
	W: AU, BR,	CA, JP, MX, US		
	RW: AT, BE,	CH, CY, DE, DK,	ES, FI, FR, GB, GR, IE,	IT, LU, MC, NL,
	PT, SE			
	US 5866602	A 19990202	US 1997-878031	19970618
	AU 9878101	A1 19990104	AU 1998-78101	19980603
PRAI	US 1997-878031	19970618		
	WO 1998-US11340	19980603		
os	MARPAT 130:66325	5		
GT				

$$Q^{1} = W$$
 $Q = W$
 $Q = W$
 $Q^{1} = W$

AB Keto-substituted THF analogs of prostaglandins I (R1 = H, C1-5-alkyl, C3-6-cycloalkyl, cationic salt moiety; A = CH2CH=CH (cis olefin), CH=CHCH2 (cis olefin), CH2CH2CH2; Z = C.tplbond.C, trans-CH=CH; one of R2 and R3 = H and the other = F or OH, the OH may be free or functionally modified; R2R3 = OCH2CH2O, O; R4 = (CH2)mXPh, (CH2)pZ; m = 1-6, X = O, CH2, the Ph may be substituted with R5, R5 = halo, Me, CF3, cyano, MeO, acetyl; p = 0-6, Z = Q, Q1; W = O, CH2, CH2CH2, CH=CH) were prepared for treatment of glaucoma and ocular hypertension. Thus the tetrahydrofuranylheptanoate derivative II was prepared in 8 steps from the alc. III via the tetrahydrofuranylheptanoate derivative IV. Pharmaceutical formulations containing

0.01 and 0.003 wt% II were prepared

ST furanylheptanoate tetrahydro prepn ocular hypotensive; tetrahydrofuranylheptanoate prepn ocular hypotensive; THF prostaglandin analog prepn ocular hypotensive IT Antiglaucoma agents Glaucoma (disease)

(preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

IT Prostaglandins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

IT 217939-71-4P 217939-72-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

IT 17814-85-6, (4-Carboxybutyl)triphenylphosphonium bromide 40665-68-7, Dimethyl 3-phenoxy-2-oxopropylphosphonate 192991-95-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

IT 208180-29-4P 217939-65-6P 217939-66-7P 217939-67-8P 217939-68-9P 217939-69-0P 217939-70-3P 217939-73-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Chembro Holdings PTY Ltd; DE 2618861 A 1976 HCAPLUS
- (2) Pfizer; GB 1539364 A 1979 HCAPLUS
- (3) Stjernschantz, J; WO 9526729 A 1995 HCAPLUS

IT 217939-71-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of keto-substituted THF analogs of prostaglandins as ocular hypotensives)

RN 217939-71-4 HCAPLUS

CN L-lyxo-Oct-5-en-2-ulose, 1,4-anhydro-3,5,6-trideoxy-3-[7-(1-methylethoxy)-7-oxoheptyl]-8-O-phenyl-, (5E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

```
ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
L11
    1998:341542 HCAPLUS
AN
DN
    129:41028
    Entered STN: 06 Jun 1998
ED
    Preparation of cis-\Delta 4 analogs of prostaglandins as ocular
TI
    hypotensives
    Klimko, Peter G.; Zinke, Paul W.
IN
    Alcon Laboratories, Inc., USA; Klimko, Peter G.; Zinke, Paul W.
PA
     PCT Int. Appl., 48 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
    English
     ICM C07C405-00
IC
     26-3 (Biomolecules and Their Synthetic Analogs)
CC
     Section cross-reference(s): 2, 63
FAN.CNT 1
                                          APPLICATION NO. DATE
     PATENT NO.
                     KIND DATE
                                           _____
                                          WO 1997-US20857 19971107
                            19980522
     WO 9821182
                      A2
PΙ
                           19980625
     WO 9821182
                      A3
         W: AU, CA, CN, JP, KR, MX, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                                                           19971107
                                          AU 1998-54393
                      A1
                            19980603
     AU 9854393
                                           EP 1997-948304
                                                            19971107
                      A2
                            19990929
     EP 944593
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                           CN 1997-199645
                                                            19971107
                            19991201
     CN 1237157
                       Α
                                           JP 1998-522859
                                                            19971107
                            20010327
     JP 2001504122
                       T2
                            20000825
                                           KR 1999-704203
                                                            19990512
     KR 2000053228
                       Α
                            20010109
                                          BR 1999-1566
                                                            19990520
                       Α
     BR 9901566
                                          US 1999-284431 19990602
     US 6235779
                       B1
                            20010522
                            19961112
PRAI US 1996-30504P
                      P
     WO 1997-US20857
                      W
                            19971107
os
     MARPAT 129:41028
GI
```

- * STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY AVAILABLE VIA OFFLINE PRINT *
- Cis- $\Delta 4$ analogs of prostaglandins I (A = CO2R, CONR1R2, CH2OR3, AB CH2NR4R5; R = H, cationic moiety, or CO2R = ophthalmically acceptable ester moiety; R1, R2 = H, alkyl; R3 = H, acyl, alkyl: R4, R5 = H, acyl, alkyl, if one of R4, R5 = acyl then the other = H or alkyl; n = 0, 2; L =OR6 in the α configuration where R6 = H, alkyl, acyl; R7 = H, alkyl, acyl; D, D1 = H, OR8, R8 = H, alkyl, acyl; X = (CH2)m, (CH2)mO, m = 1-6; Y= (un) substituted phenyl; XY = (CH2)pY1; p = 0-6; W = CH2, O, S, SO, SO2, NR9, CH:CH, CH2O, CH2S, CH2SO, CH2SO2, CH:N, CH2NR9; R9 = H, alkyl, acyl; Z = H, alkyl, alkoxy, acyl, acyloxy, halo, trihalomethyl, amino, alkylamino, acylamino, OH) were prepared for treatment of glaucoma and ocular hypertension. Thus, the diol II underwent tetrahydropyranylation, reduction and Wittig reaction with Ph3P+CH2OMe Cl- followed by cyclization to give the corresponding lactol, which underwent Wittig reaction with Ph3P+CH2CH2CH2CO2H Br- to give the tetranorprostadienoic acid III. Ophthalmic formulations containing 0.001% III were prepared prostaglandin prepn ocular hypotensive; glaucoma treatment prostaglandin ST

Antiglaucoma agents (preparation of cis-∆4 analogs of prostaglandins as ocular hypotensives)

IT

Prostaglandins IT RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of $cis-\Delta 4$ analogs of prostaglandins as ocular hypotensives) 208115-11-1P 208180-50-1P 208112-13-4P 192992-28-2P IT 208180-54-5P 208180-52-3P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of $\operatorname{cis-}\Delta 4$ analogs of prostaglandins as ocular hypotensives) 110-87-2, 3,4-Dihydro-2H-pyran 4009-98-7 17857-14-6 39746-01-5 IT 178454-81-4 192991-95-0 54094-19-8 53872-60-9 53273-61-3 RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of $cis-\Delta 4$ analogs of prostaglandins as ocular hypotensives) 130386-85-5P 71358-54-8P 84786-80-1P 105674-66-6P IT39746-00-4P 192992-23-7P 192992-24-8P 192992-25-9P 192992-22-6P 208111-93-7P 208111-90-4P 208111-91-5P 208111-92-6P 208111-89-1P 208114-22-1P 208111-96-0P 208111-97-1P 208114-21-0P 208111-94-8P 208114-43-6P 208114-44-7P 208114-42-5P 208114-40-3P 208114-41-4P 208180-17-0P 208180-18-1P 208114-47-0P 208114-45-8P 208114-46-9P 208180-25-0P 208180-22-7P 208180-21-6P 208180-20-5P 208180-19-2P 208180-30-7P 208180-28-3P 208180-29-4P 208180-27-2P 208180-26-1P 208252-64-6P 208180-62-5P 208180-34-1P 208180-35-2P 208180-37-4P 208252-65-7P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of $cis-\Delta 4$ analogs of prostaglandins as ocular hypotensives) IT 192992-28-2P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of cis- $\Delta 4$ analogs of prostaglandins as ocular hypotensives) RN 192992-28-2 HCAPLUS L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-CN [(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

L11 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN AN 1998:323138 HCAPLUS

```
129:19683
DN
     Entered STN: 30 May 1998
ED
     Use of a combination of carbonic anhydrase inhibitors and prostaglandins
TI
     for treating glaucoma
     Dean, Thomas R.; May, Jesse A.
IN
     Alcon Laboratories, Inc., USA; Dean, Thomas R.; May, Jesse A.
PA
     PCT Int. Appl., 22 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
     ICM A61K031-557
IC
     ICS A61K031-54
     63-6 (Pharmaceuticals)
     Section cross-reference(s): 1
FAN.CNT 1
                                           APPLICATION NO. DATE
                      KIND DATE
     PATENT NO.
     _____
                                            _____
                     ----
                      A1 19980514
                                           WO 1997-US15793 19970905
     WO 9819680
PΙ
         W: AU, CA, JP, MX, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                      A1 19980529
                                          AU 1997-42573
                                                             19970905
     AU 9742573
     AU 734789
                       B2
                            20010621
                                           EP 1997-940895
                                                             19970905
     EP 948333
                       A1
                            19991013
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                            20010327
                                            JP 1998-521363
                                                             19970905
     JP 2001504100
                       T2
                                                             19990430
                                            MX 1999-4069
                       Α
                             20000531
     MX 9904069
                             19961101
PRAI US 1996-29538P
                       Р
                      W
                            19970905
     WO 1997-US15793
     Compns. for treating persons suffering from glaucoma or ocular
AΒ
     hypertension consist of prostaglandins and carbonic anhydrase inhibitors.
     Thus, an ophthalmic composition (pH 7.1) contained brinzolamide 1.0, (+)-isopropylfluprostenol 0.005, HPMC 0.5, dibasic sodium phosphate 0.2,
     disodium edetate 0.01, NaCl 0.8, benzalkonium chloride 0.01, and Cremaphor
     0.1%, and purified water qs.
     antiglaucoma prostaglandin carbonic anhydrase inhibitor
ST
     Antiglaudoma agents
TT
        (carbonic anhydrase inhibitors and prostaglandins for treatment of
        glaucoma)
IT
     Prostaglandins
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
         (carbonic anhydrase inhibitors and prostaglandins for treatment of
        qlaucoma)
     Drug delivery systems
IT
         (ophthalmic; carbonic anhydrase inhibitors and prostaglandins for
        treatment of glaucoma)
                                  157283-68-6 192992-28-2
     138890-62-7, Brinzolamide
IT
     207670-11-9
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
      (Uses)
         (carbonic anhydrase inhibitors and prostaglandins for treatment of
        glaucoma)
      9001-03-0, Carbonic anhydrase
IT
      RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (inhibitors; carbonic anhydrase inhibitors and prostaglandins for
         treatment of glaucoma)
              THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 11
```

RE

(1) Alcon Lab Inc; EP 0590786 A 1994 HCAPLUS

- (2) Alcon Lab Inc; WO 9723223 A 1997 HCAPLUS
- (3) Alcon Laboratories Inc; EP 0667160 A 1995 HCAPLUS
- (4) Alcon Laboratories Inc; US 5378703 A 1995 HCAPLUS
- (5) Bishop, J; US 5510383 A 1996 HCAPLUS
- (6) Hoyng; SURVEY OF OPHTHALMOLOGY 1997, V41(S2), PS93
- (7) Merck & Co; CN 1075634 A 1993
- (8) Merck & Co; Ophthalmic Compositions Comprising Combinations of a Carbonic Anhydrase Inhibitor and a Prostaglandin or Prostaglandin Derivative 1993
- (9) Pfeiffer, N; CURRENT OPINION IN OPHTHALMOLOGY 1994, V5(2), P20
- (10) Ueno Seiyaku Oyo Kenkyujo Kk; EP 0501678 A 1992 HCAPLUS
- (11) Von der Eltz; PHARMAZEUTISCHE ZEITUNG 1996, V141(8), P11 HCAPLUS
- IT 192992-28-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(carbonic anhydrase inhibitors and prostaglandins for treatment of glaucoma)

- RN 192992-28-2 HCAPLUS
- CN L-altro-Oct-3-enitol, 5,8-anhydro-1-O-(3-chlorophenyl)-3,4,6-trideoxy-6-[(3Z)-7-(1-methylethoxy)-7-oxo-3-heptenyl]-, (3E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

- L11 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
- AN 1997:503170 HCAPLUS
- DN 127:135678
- ED Entered STN: 09 Aug 1997
- TI Preparation of substituted tetrahydrofuran analogs of prostaglandins as ocular hypotensives
- IN Selliah, Robert D.; Hellberg, Mark R.; Klimko, Peter G.; Sallee, Verney
 L.; Zinke, Paul W.
- PA Alcon Laboratories, Inc., USA; Selliah, Robert D.; Hellberg, Mark R.; Klimko, Peter G.; Sallee, Verney L.; Zinke, Paul W.
- SO PCT Int. Appl., 64 pp. CODEN: PIXXD2
- DT Patent
- LA English
- IC ICM A61K031-557

ICS C07D307-18; C07D307-20; C07D307-80; C07D407-06

CC 26-3 (Biomolecules and Their Synthetic Analogs) Section cross-reference(s): 1, 63

FAN.CNT 2

PATENT NO. KIND DATE APPLICATION NO. DATE

```
PΙ
     WO 9723223
                        A1
                             19970703
                                             WO 1996-US17900 19961112
         W: AU, CA, CN, JP, MX, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     CA 2236582
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                        Α1
                             19970717
                                             AU 1996-76106
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                        B2
                             19991223
     EP 869794
                                             EP 1996-938819
                        Α1
                             19981014
                                                               19961112
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     CN 1205638
                        Α
                             19990120
                                             CN 1996-199181
                                                               19961112
     JP 3032302
                        B2
                             20000417
                                             JP 1997-523627
                                                               19961112
     US 5994397
                             19991130
                                             US 1997-809920
                        Α
                                                               19970404
     US 6025392
                             20000215
                                             US 1998-109852
                        Α
                                                               19980702
     US 6197812
                        B1
                             20010306
                                             US 1999-440248
                                                               19991115
     US 2001029265
                        A1
                             20011011
                                             US 2001-800179
                                                               20010306
     US 6369102
                        В2
                             20020409
PRAI US 1995-9866P
                        Р
                             19951222
     WO 1996-US17900
                        W
                             19961112
     US 1997-809920
                        A2
                             19970404
     US 1999-440248
                        Α1
                             19991115
os
     MARPAT 127:135678
GI
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HO

Y (CH₂) 2 (CH₂) nR

$$ZCR^2R^3R^4$$

HO

 CO_2CHMe_2

OH

 $C1$

III

- AB Prostaglandin THF analogs I and II [R = CO2R1, CONR7R8, CH2OR9, CH2NR10R11; R1 = H, cationic salt moiety; R7 = R8 = H, alkyl; R9 = R10 = R11 = H, acyl, alkyl; Y = (Z)-CH2CH:CH, (Z)-CH:CHCH2, (CH2)3; Z = (E)-CH:CH, (CH2)2, C.tplbond.C; Y2 = halogen, alkoxy; X2 = O, S, CH2; A = (Z)-CH:CH, (CH2)2, C.tplbond.C; R2 = R3 = H, F, OH; R2R3 = O, protected carbonyl; R4 = cyclohexyl, alkyl] were prepared for use in treating glaucoma and ocular hypertension (no data). Thus, prostaglandin analog III was prepared in a multistep synthesis starting from 1,2-O-isopropylidene- α -D-xylofuranose.
- ST prostaglandin THF analog prepn ocular hypertension; glaucoma agent prostaglandin THF analog prepn; oxaprostaglandin prepn glaucoma agent ocular hypertension
- IT Antihypertensives
 - RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (ocular; preparation of substituted THF analogs of prostaglandins as ocular hypotensives)
- IT Antiglaucoma agents

```
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of substituted THF analogs of prostaglandins as ocular
        hypotensives)
IT
     Prostaglandins
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
         (prostanoids; preparation of substituted THF analogs of prostaglandins as
        ocular hypotensives)
IT
     98-88-4, Benzoyl chloride
                                 108-98-5, Thiophenol, reactions
                                                                     867-13-0,
                               4009-98-7, (Methoxymethyl)triphenylphosphonium
     Triethylphosphonoacetate
               17814-85-6, (4-Carboxybutyl) triphenylphosphonium bromide
     17857-14-6, (3-Carboxypropyl)triphenylphosphonium bromide 29921-57-1, Isopropyl bromoacetate 40665-94-9 58009-66
                                                         58009-66-8
                                                                      88738-78-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of substituted THF analogs of prostaglandins as ocular
        hypotensives)
IT
     6022-96-4P
                  6698-46-0P
                               58399-68-1P
                                             77772-47-5P
                                                             80923-96-2P
     192991-91-6P
                    192991-92-7P
                                    192991-93-8P
                                                   192991-94-9P
                                                                   192991-95-0P
     192991-98-3P
                    192992-00-0P
                                    192992-02-2P 192992-03-3P
     192992-04-4P 192992-05-5P 192992-06-6P 192992-07-7P
     192992-08-8P
                    192992-09-9P
                                    192992-10-2P
                                                    192992-11-3P
                                                                   192992-12-4P
     192992-13-5P
                    192992-14-6P
                                    192992-15-7P
                                                    192992-16-8P
                                                                   192992-17-9P
     192992-18-0P
                    192992-19-1P
                                    192992-20-4P
                                                    192992-21-5P
                                                                   192992-22-6P
     192992-23-7P 192992-24-8P 192992-25-9P
                                               192992-30-6P
     193075-40-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of substituted THF analogs of prostaglandins as ocular
        hypotensives)
TT
     113428-35-6P 192992-26-0P
                                  192992-27-1P
     192992-28-2P
                    192992-29-3P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of substituted THF analogs of prostaglandins as ocular
        hypotensives)
IT
     192992-03-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of substituted THF analogs of prostaglandins as ocular
        hypotensives)
RN
     192992-03-3 HCAPLUS
CN
     D-ribo-Oct-5-enitol, 1,4-anhydro-8-O-(3-chlorophenyl)-3,5,6-trideoxy-3-
     [(2Z)-7-methoxy-7-oxo-2-heptenyl]-7-0-(tetrahydro-2H-pyran-2-yl)-,
     (5E,7\xi) - (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

Double bond geometry as shown.

L11 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1988:131340 HCAPLUS

DN 108:131340

ED Entered STN: 15 Apr 1988

TI Synthesis of methyl (5Z,13E) (15S)-9 α -acetoxy-15-hydroxy-17-(3-trifluoromethylphenyl)-11-oxa-18,19,20-trinorprosta-5,13-dienoate

AU Verdoorn, Gerhard H.; Holzapfel, Cedric W.; Koekemoer, Johannes M.

CS Dep. Chem., Rand Afrikaans Univ., Johannesburg, 2000, S. Afr.

SO South African Journal of Chemistry (1987), 40(2), 134-8 CODEN: SAJCDG; ISSN: 0379-4350

DT Journal

LA English

CC 26-3 (Biomolecules and Their Synthetic Analogs)

GI

AB The title compound (I) was prepared from D-glucose. A key step in the synthesis was the deoxygenation of the furanose II (R = OH) by reaction with MeSO2Cl and NaBH3CN reduction of II (R = Cl). An improved method for the introduction of the ω -side chain utilizes the orthoester III.

```
ST
     oxatrinorprostadienoate; prostaglandin oxa
     Prostaglandins
IT
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (oxatrinorprostadienoates, preparation of)
IT
     779-89-5, 3-Trifluoromethylcinnamic acid
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (hydrogenation of)
     58399-55-6
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (hydrolysis of)
TT
     70783-99-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and Wittig reaction of, with tetrahydrofurancarboxaldehyde)
IT
     113531-01-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and acetylation of)
IT
     585-50-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and chlorination of)
IT
     113331-70-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and dehydroxylation of)
IT
     113331-72-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and deisopropylidenation of)
     113331-74-1P
IT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydrolysis of)
IT
     113331-78-5P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and oxidation of)
IT
     113331-71-8P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, with carboxybutyltriphenylphosphonium bromide)
     113331-73-0P
IT
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, with dioxabicyclooctanol)
IT
    113331-75-2P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, with methoxide)
     455-03-8P, 3-(3-Trifluoromethylphenyl)propionyl chloride
IT
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, with methylphosphonate)
IT
    113331-77-4P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction of, with triphenylphosphine)
IT
    113331-76-3P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
```

```
(preparation and rearrangement of)
IT
     101069-36-7P 113331-79-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reduction of)
     113331-80-9P 113428-35-6P
IT
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of)
     3143-02-0, 3-Hydroxymethyl-3-methyloxetane
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with bromovaleryl chloride)
     17814-85-6, 4-Carboxybutyltriphenylphosphonium bromide
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with dioxabicyclooctanol)
     4509-90-4, 5-Bromovaleryl chloride
TТ
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with hydroxymethylmethyloxetane)
IT
     756-79-6, Dimethyl methylphosphonate
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with trifluoromethylphenylpropionyl chloride)
IT
     113331-79-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reduction of)
     113331-79-6 HCAPLUS
RN
     5-Heptenoic acid, 7-[4-(acetyloxy)tetrahydro-2-[3-oxo-5-[3-
CN
     (trifluoromethyl)phenyl]-1-pentenyl]-3-furanyl]-, methyl ester,
     [2R-[2\alpha(E),3\beta(Z),4\beta]]-(9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

Double bond geometry as shown.

```
L11
    ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN
     1986:186178 HCAPLUS
AN
DN
     104:186178
     Entered STN: 01 Jun 1986
ED
ΤI
     Total synthesis of 11-oxaprostaglandin F2\alpha and F2\beta
     Hanessian, Stephen; Guindon, Yvan; Lavallee, Pierre; Dextraze, Pierre
ΑU
     Dep. Chem., Univ. Montreal, Montreal, QC, H3C 3V1, Can.
CS
SO
     Carbohydrate Research (1985), 141(2), 221-38
     CODEN: CRBRAT; ISSN: 0008-6215
     Journal
DT
LΑ
     English
     26-3 (Biomolecules and Their Synthetic Analogs)
CC
     Section cross-reference(s): 33
os
     CASREACT 104:186178
GI
```

AB Title compds. I and II and their C-15 epimers were synthesized from 1,4-anhydro-D-glucitol. Also prepared were chiral THF derivs. such as III and IV. I and II did not show smooth-muscle contracting ability. STanhydroglucitol oxa prostaglandin synthon; glucitol anhydro prostaglandin synthon IT Synthons (anhydroglucitol, for prostaglandin oxa analogs) TΤ Prostaglandins RL: RCT (Reactant); RACT (Reactant or reagent) (analogs, PGF2 oxa, total synthesis of, from anhydroglucitol) ITRL: RCT (Reactant); RACT (Reactant or reagent) (Wittig condensation of, in synthesis of oxa prostaglandins) IT 105-53-3 RL: RCT (Reactant); RACT (Reactant or reagent) (alkylation with, in synthesis of oxa prostaglandins from anhydroglucitol) IT55730-76-2P 101144-12-1P 101144-18-7P RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and alkylation with di-Et malonate) IT 55285-66-0P 55730-81-9P **101069-33-4P** 101069-52-7P 101069-55-0P 101144-16-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and borohydride reduction of) IT 55730-79-5P 101069-39-0P RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and conversion into acetonide)

```
IT
      55730-74-0P
      RL: SPN (Synthetic preparation); PREP (Preparation)
          (preparation and conversion into epoxide)
      101069-30-1P 101069-36-7P 101069-45-8P
                                                   101069-62-9P
 IT
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
       (Reactant or reagent)
          (preparation and deprotection of)
                     101069-44-7P 101144-06-3P
 IT
      101069-34-5P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
       (Reactant or reagent)
          (preparation and desilylation of)
                     101069-43-6P
                                                   101069-51-6P
 IT
      101069-35-6P
                                    101069-50-5P
                                                                   101069-60-7P
      101069-61-8P
                     101144-15-4P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
       (Reactant or reagent)
          (preparation and esterification of)
 IT
      101144-07-4P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
       (Reactant or reagent)
         (preparation and hydride reduction of)
 IT
      101069-27-6P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
          (preparation and hydrogenation of)
 IT
      101069-26-5P
      RL: SPN (Synthetic preparation); PREP (Preparation)
         (preparation and oxidation to ketone)
 IT
                    101069-49-2P 101069-58-3P
                                                   101069-59-4P
      101069-48-1P
                                                                   101144-14-3P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation and partial decarboxylation of)
 IT
      59286-02-1P
                    101069-31-2P
                                   101069-37-8P
                                                 101069-46-9P
                                                                  101069-54-9P
      101222-38-2P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation and periodate oxidation of)
 IT
      101069-29-8P
                    101069-42-5P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation and reaction with (carboxybutyl)triphenylphosphonium bromide)
                    101069-32-3P 101069-38-9P 101069-47-0P
IT
      58399-68-1P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation and reaction with (tributylphosphoranylidene)heptanone)
 IT
      101125-99-9P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation and reaction with [(ethoxycarbonyl)methylene]triphenylphosphora
         ne)
 IT
      55730-77-3P
                    55730-78-4P
                                 61876-91-3P
                                                61914-86-1P
                                                               101069-56-1P
                    101144-08-5P
                                   101144-09-6P
      101069-57-2P
                                                  101144-13-2P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation and saponification of)
 TΤ
      101069-41-4P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation and silylation of)
 IT
      101069-28-7P
```

RL: SPN (Synthetic preparation); PREP (Preparation)

```
(preparation and use in synthesis of oxa prostaglandins)
    55730-73-9P
IT
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and use of, in synthesis of oxa prostaglandins)
    55730-75-1P 58399-69-2P
IT
                                101069-40-3P 101069-53-8P 101069-63-0P
                  101144-17-6P
    101126-00-5P
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of)
IT
    25952-53-8
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with anhydroglucitol derivative)
IT
    27299-12-3P
    RL: PREP (Preparation)
        (starting material for synthesis of oxa prostaglandins)
    58399-72-7P 58437-46-0P 101144-10-9P 101144-11-0P
IT
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (total synthesis of, from anhydroglucitol)
IT
    1099-45-2 17814-85-6 35563-52-1
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (use of, in synthesis of oxa prostaglandins)
IT
    101069-33-4P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and borohydride reduction of)
    101069-33-4 HCAPLUS
RN
    5-Heptenoic acid, 7-[4-[[(1,1-dimethylethyl)diphenylsilyl]oxy]tetrahydro-2-
CN
```

Absolute stereochemistry.

Double bond geometry as shown.

1978:405999 HCAPLUS

Entered STN: 12 May 1984

89:5999

AN DN

ED

(3-oxo-1-octenyl)-3-furanyl]-, methyl ester, [2R-

L11 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2004 ACS on STN

 $[2\alpha(E), 3\beta(Z), 4\beta]$] - (9CI) (CA INDEX NAME)

```
11-Deoxy-11-oxaprostaglandin compounds
TI
    Corey, Elias James; Eggler, James Frederick
IN
    Pfizer Inc., USA
PΑ
SO
    Ger. Offen., 49 pp.
    CODEN: GWXXBX
DT
    Patent
LA
    German
IC
    C07D307-32
CC
    24-4 (Alicyclic Compounds)
    Section cross-reference(s): 27, 63
FAN.CNT 1
    PATENT NO.
                    KIND DATE
                                           APPLICATION NO. DATE
```

ΡI	DE	2739277	A1	19780316	DE	1977-2739277	19770831
	DE	2739277	C2 *	19820609			
	JP	53037653	A2	19780406	JP	1977-109398	19770910
	JP	57055719	B4	19821125			
	BE	858682	A1	19780314	BE	1977-180893	19770914
	DK	7704083	Α	19780316	DK	1977-4083	19770914
	NL	7710065	Α	19780317	NL	1977-10065	19770914
	NL	169739	В	19820316			
	NL	169739	C	19820816			
	FR	2364912	A1	19780414	FR	1977-27747	19770914
	FR	2364912	B1	19801003			
	GB	1539364	Α	19790131	GB	1977-38389	19770914
PRAI	US	1976-723604		19760915			
GT			•				

AB I (Q = carboxy or tetrazolyl, R1,R2 = H, OH; R3 = H, Cl, F, Me, MeO, CF3, A = CH2CH2 or cis-CH:CH, and Z = CH2CH2 or trans CH:CH) were prepared Thus, 1,2:5,6-diisopropylidene-D-mannitol was treated with Pb(OAc)4 to give YCHO (Y = 2,2-dimethyl-1,3-dioxolan-4-yl), which with (MeO)2P(O)CH2CO2Me gave YCH:CHCO2Me; this was vinylated and lactonized to give II, which was incorporated into conventional prostaglandin synthesis procedures to give ent-prostaglandin analogs, e.g., III.

ST prostaglandin oxa ent

IT Prostaglandins

RL: RCT (Reactant); RACT (Reactant or reagent)
 (11-oxa analogs)

IT 1707-77-3

RL: RCT (Reactant); RACT (Reactant or reagent)
 (lead tetraacetate cleavage of)

IT 917-57-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(metalation-addition reaction of, with dioxolanylacrylate derivative)

IT 66601-86-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and borohydride reduction of)

IT 66601-88-5P 66674-02-0P

```
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydride reduction of)
IT
     66601-92-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydrogenation of)
ΙT
     66601-91-0P 66674-04-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydrolysis or hydrogenation of)
IT
     66601-82-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and metalation-addition reaction with vinyllithium)
ΙT
     58399-67-0P 58399-67-0P 66601-90-9P 66674-03-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and oxidation of)
IT
     66601-84-1P
                  66601-85-2P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and oxidation with 3-chloroperbenzoic acid)
     66601-87-4P
IT
                  66674-01-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and protection with dihydropyran)
IT
     66601-89-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction with (4-carboxybutyl)triphenylphosphonium bromide)
IT
     66673-99-2P
                   66674-00-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction with di-Me [2-oxo-3-(3-
        methylphenyl)propyl]phosphonate)
IT
     15186-48-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reaction with tri-Me phosphonoacetate)
TΤ
     66601-83-0P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and use in oxaprostaglandin synthesis)
     66601-93-2P 66674-05-3P
TT
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of)
IT
     5927-18-4
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with isopropylideneglyceraldehyde)
IT
                  61263-05-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (use of, in oxaprostaglandin synthesis)
TI
     66601-92-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydrogenation of)
RN
     66601-92-1 HCAPLUS
     3-Furanheptanoic acid, tetrahydro-2-[4-(3-methylphenyl)-3-[(tetrahydro-2H-
CN
     pyran-2-yl)oxy]-1-butenyl]-4-oxo-, [2S-[2\alpha,(1E,3R*),3\beta]]-(9CI)
       (CA INDEX NAME)
```

=> b home FILE 'HOME' ENTERED AT 16:13:41 ON 30 JUN 2004